METHOD

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DRUG DISCOVERY

Design, ultrasound assisted Synthesis and anticancer screening of 4-[5-(aryl)-4, 5-dihydro-1H-pyrazol-3-yl]-3-(substituted phenyl) sydnones

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Present research work focused to green synthesis of novel mesoionic compounds containing sydnone moiety and their anticancer screening. Scheme 1shows synthesis of compounds 4-[5-(aryl)-4, 5-dihydro-1H-pyrazol-3-yl]-3-(substituted phenyl) sydnones (2a-j) by cyclization of sydnonyl-substituted α, β-unsaturated ketones (1a-j) with hydrazine hydrate. All compounds were characterized by spectral studies. Molecules 2i, 2j were evaluated against 60 human cancer cell lines for *in vitro* anticancer activity. A compound 2i was found to have greater anticancer activity than standard vincristine sulphate against specific cell lines. Further structural modification of the active mesoionic sydnones might lead to development of potent anticancer molecules.

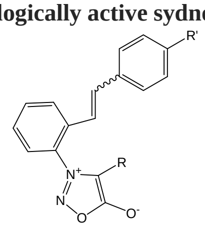
INTRODUCTION

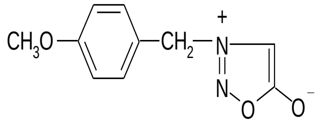
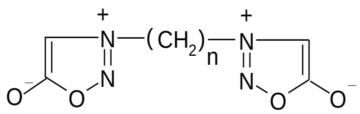
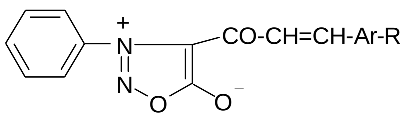
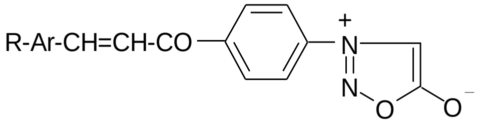
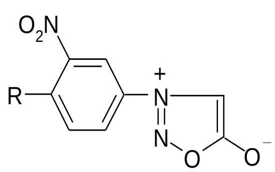
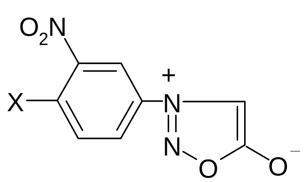
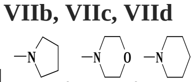
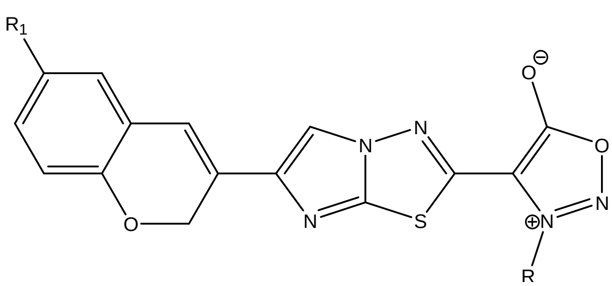
Cancer is a leading cause of death in the world and tightening its grip with the increase in mortality rate day by day. The mortality rates due to cancer are likely to increase to a great extent by 2020. The word cancer refers to “abnormal and uncontrolled growth of cells” and antineoplastic means “against new growth”. Most of the anti-neoplastic agents act by interfering with cellular synthesis or functioning of DNA/RNA or proteins. (Lemke et al, 2008).

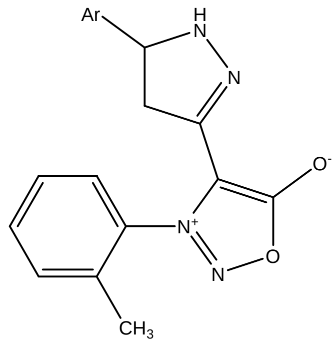
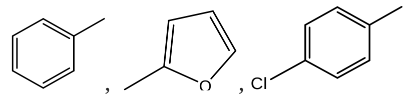
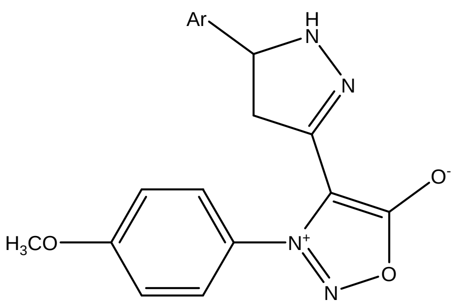
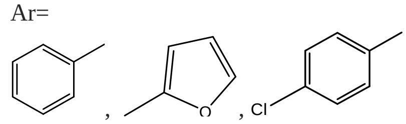
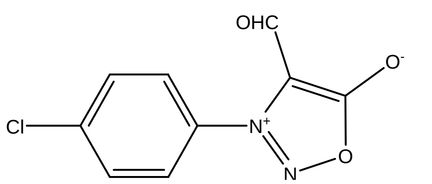
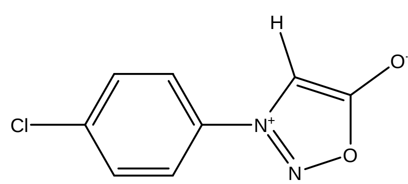
Sydnonesas anticancer agents

Mesoionicsydnone derivatives have been described for a variety of antitumor activities (Butkovic et al, 2011; Grynberg et al, 1992; Greco et al, 1962; Satyanarayana et al, 2004; Satyanarayana et al, 1995; Dunkley et al, 2003; Dunkley et al, 2003; Tegginamath et al, 2013; Bhosale et al, 2015; Bhosale et al, 2015; Bhosale et al, 2017). It has been observed that the ionic resonance structure of sydnone ring enhances interactions with cancer cells. Based on literature survey and reported antitumor molecules we have designed and synthesized molecule **2a-j.**

Table 1 Reported sydnones and their derivatives having antitumor activity
(Butkovic et al, 2011; Grynberg et al, 1992; Greco et al, 1962; Satyanarayana et al, 2004; Satyanarayana et al, 1995; Dunkley et al, 2003; Dunkley et al, 2003; Tegginamath et al, 2013; Bhosale et al, 2015; Bhosale et al, 2015; Bhosale et al, 2017)

Biologically active sydnones	Substituents	Biological activity	Ref.
 **Ia, Ib**	**Ia**R=CH_3, R’=CH_3 **Ib** R=Ph, R’=Cl cis-4-methyl-3-[2-[2-(4-methylphenyl) ethenyl] phenyl] sydnone (**Ia)** cis-4-phenyl-3-[2-[2-(4-chlorophenyl)ethenyl]-phenyl] sydnone (**Ib)**	Anticancer	01

 **II**	3-(p-methoxybenzyl) sydnone	Anticancer against carcinoma-755	02
 **III**	polymethylene-bis-sydnones	Potent antitumor	03
 **IV**	**IVa**Ar= Ph, R=4-CH_3 **IVb**Ar= Ph, R=3-OCH_3, 4-OH, **IVc**Ar= Ph, R=4-CF_3	Highly selective against SNB-75 tumour cell line of CNS	04
 **V**	**Va**Ar=Ph, R= H, **Vb**Ar=Ph, R=4CH_3,**Vc** Ar=Ph, R=4-OCH_3, **Vd**Ar=PH, R=2,4-$(OCH_3)_2$, **Vg** Ar=Ph, R=3- Cl, **Vh**Ar=Ph, R=2-Cl **Ve**Ar=Ph, R=4-$NHCOCH_3$, **Vf**Ar=Ph, R=4-Cl, **Vg**Ar=Ph, R=3-Cl,**Vh** Ar=Ph, R=2-Cl	Anticancer	04,05
 **VI**	**VI**R=F 4-substituted-3-nitrophenyl sydnone	Anticancer against MCF7 (Breast), NCI-H460 (Lung) and SF-268 (CNS) cell lines	06, 07
 **VII**	**VIIa, VIIb, VIIc, VIId** X= Cl,  3-[4-X-3-nitrophenyl]-1,2,3-oxadiazolium-5-olates	Anticancer against Sarcoma 180, Ehrlich carcinoma, B10MCII (Fibrous histiocytoma) and L1210 leukemia ascitictumours	06, 07
 4-[6'-(caumarin-3''-yl)-imidazo-[2,1-b][1,3,4]thiadiazol-2'-yl]-3-arylsydnone, **VIII**	R_1=H ,Br, Cl, H, Br, Cl, H, Br, Cl, H, Br, Cl R= C_6H_5, C_6H_5, C_6H_5, P-CH_3-C_6H_4, P-CH_3-C_6H_4, p-CH_3-C_6H_4, P-OCH_3-C_6H_4, p-OCH_3-C_6H_4, p-OCH_3-C_6H_4, p-Cl-C_6H_4, p-Cl-C_6H_4, p-Cl-C_6H_4	Anticancer	08
	Ar=	Antitumor against human breast cancer	09

 **IX**		cell line MDA-MB-231 and human prostate cancer cell line PC3	
 **X**	Ar= 	Antitumor against non-small cell lung cancer cell line (HOP-92), melanoma (M-14) and human prostate cancer cell line (PC3)	10
 3-(4-Chlorophenyl)-4-sydnonecarboxaldehyde, **XI**	 4-chlorophenyl sydnone **XII**	Antitumor against non-small cell lung cancer cell line (NCI-H23), CNS cancer cell line (SNB-75)	11

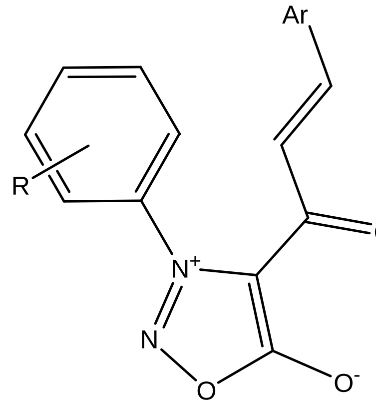
MATERIALS AND METHODS

All chemicals used from Sigma-Aldrich, Mumbai, India. Melting points were recorded on Systolic apparatus. TLC was carried out to monitor the completion of reaction by using E-Merck precoated 60 F254 plates. IR spectra were recorded by using KBr pellets on Jasco FTIR 1460. NMR spectra were recorded on a BRUKER AVANCE II 400 (are expressed in δ, ppm). MS were performed on WATERS, Q-TOF instrument. The ultra-sonication study was performed at frequency, 40 KHz.

Synthesis and characterization of 4-[5-(aryl)-4,5-dihydro-1H-pyrazol-3-yl]-3-(substitutedphenyl)sydnones 2a-j:

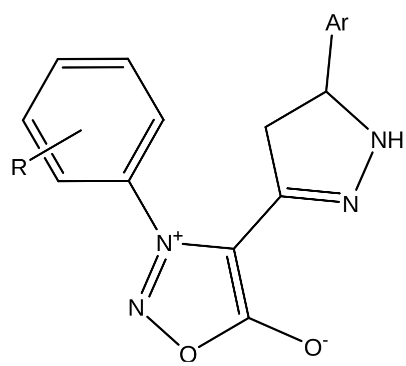
Synthesis of 4-[5-(4-methoxyphenyl)-4,5-dihydro-1H-pyrazol-3-yl]-3-(4-fluorophenyl)sydnone(2b):

To an ice cold solution of hydrazine hydrate (20mM) in ethanol(30ml), 4-[1-oxo-3-(4-methoxyphenyl)-2-propenyl]-3-(4-fluorophenyl) sydnone,**1b** (5mM) was added and heated at 60 °C for 1h under ultrasonication and then cooled. The precipitate washed in cold ethanol to obtain **2b** (135mg, Rf =0.539, Ethyl acetate: Benzene, 2:8). In similar way all remaining compounds **2a-j** were synthesized from respective **1a-j**as shown in scheme 1.

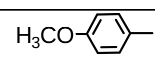
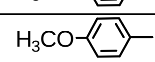
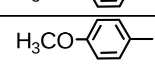
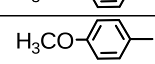
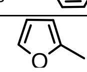
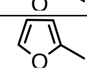
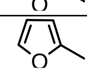
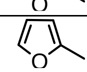
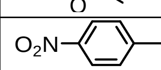
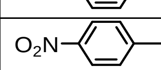


1a-j

NH_2-NH_2
1h,
Ethanol



2a-j

Comp.	R	Ar
1a, 2a,	4-Cl	
1b, 2b	4-F	
1c, 2c	2,4-Cl_2	
1d, 2d	4-Br	
1e, 2e	4-Cl	
1f, 2f	4-F	
1g, 2g	2,4-Cl_2	
1h, 2h	4-Br	
1i, 2i	4-Cl	
1j, 2j	4-F	

Scheme 1
Synthesis of 4-[5-(aryl)-4,5-dihydro-1H-pyrazol-3-yl]-3-(substituted phenyl)sydnones **2a-j** from 4-[1-oxo-3-(aryl)-2-propenyl]-3-(substitutedphenyl)sydnone, **1a-j**

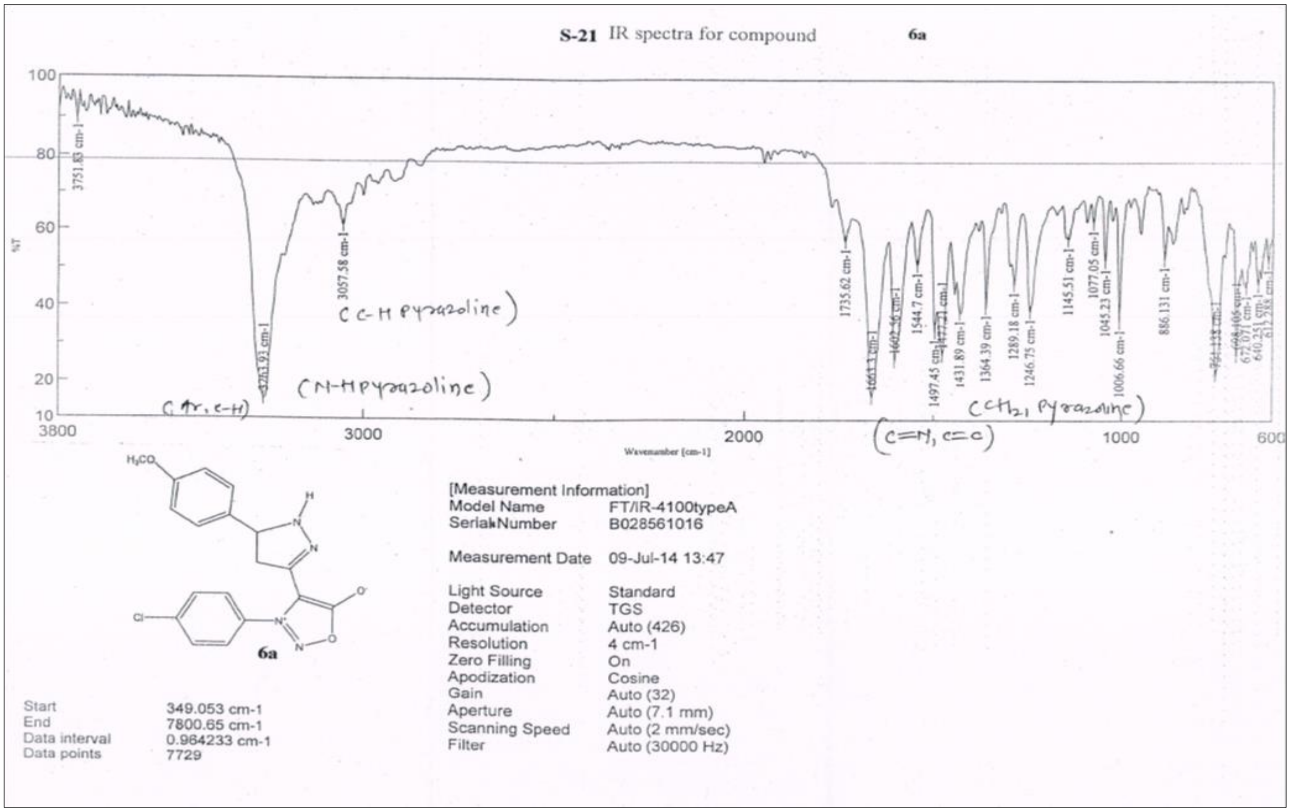


Figure 1 IR Spectrum for compound 2a

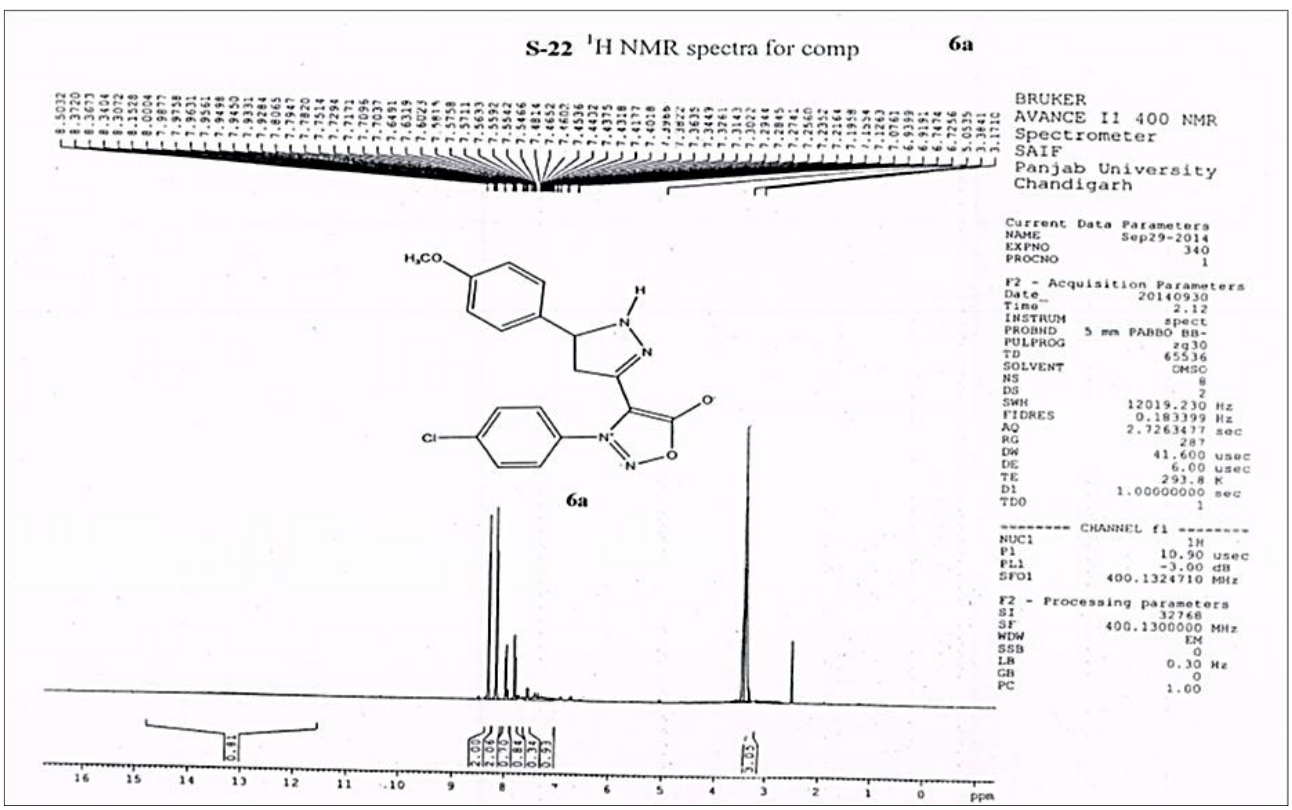


Figure 2 ^{1}H NMR Spectrum for compound 2a

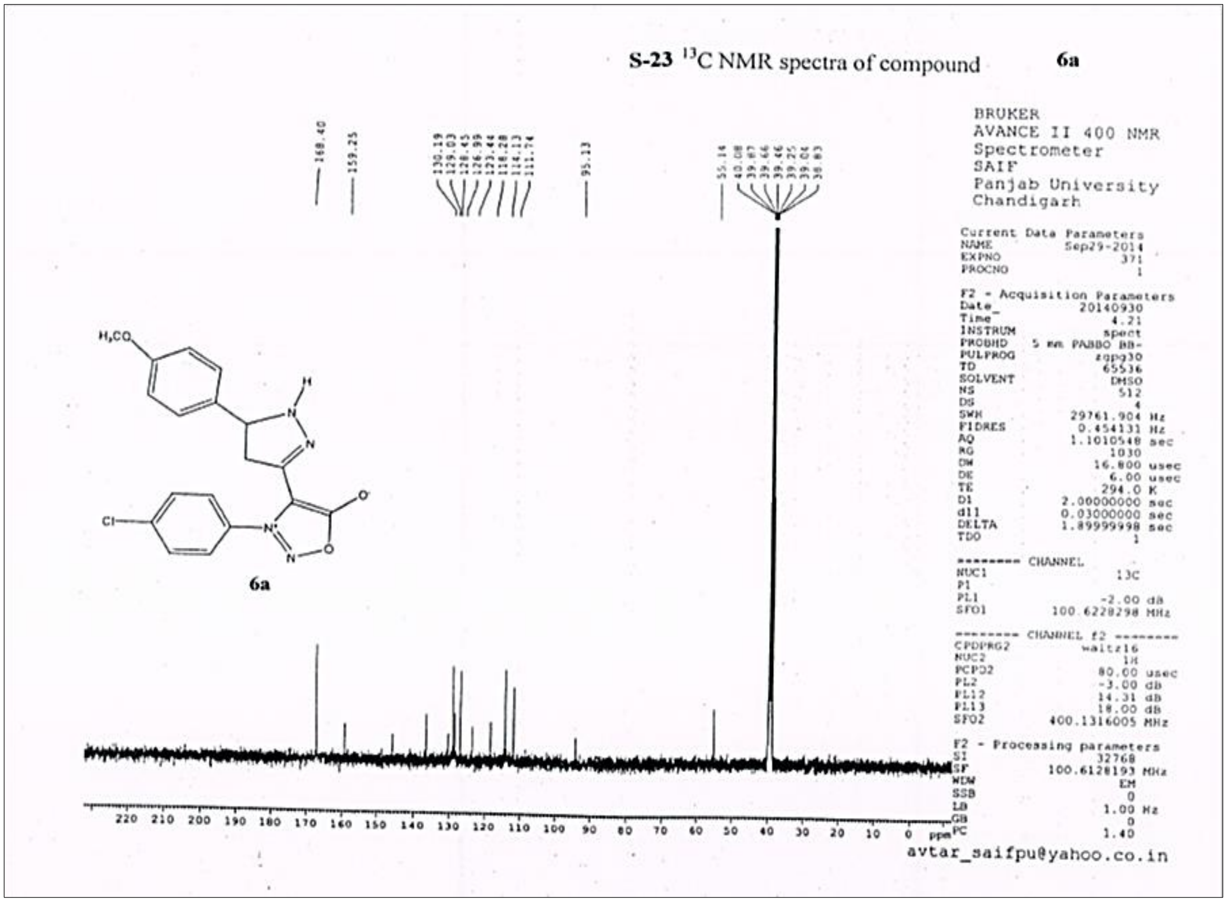


Figure 3 ^{13}C NMR Spectrum for compound 2a

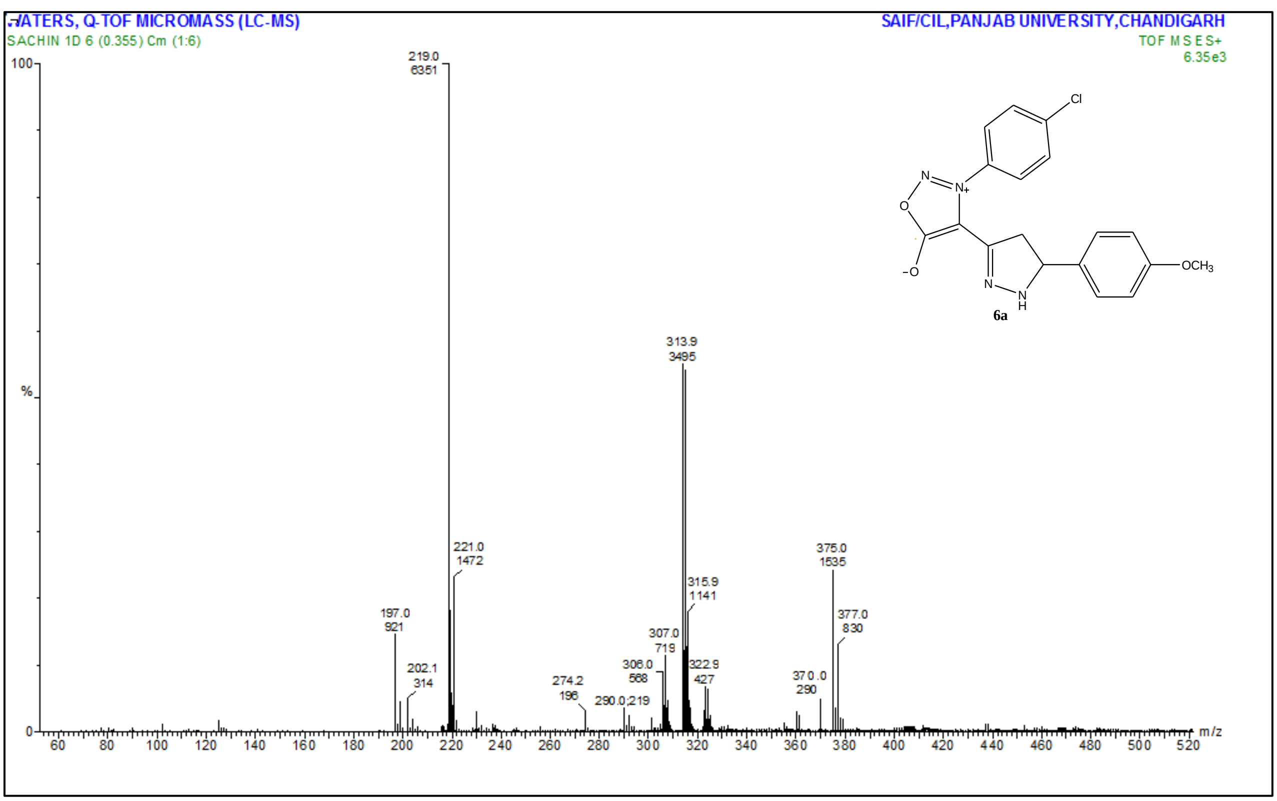


Figure 4 Mass Spectrum for compound 2a

Table 2 Characterization for compounds 2a-2j

Compound with IUPAC name	IR (KBr) (cm^{-1})	^{1}H NMR (δ ppm)	^{13}C NMR (δ ppm)	Physicochemical data
4-[5-(4-methoxyphenyl)-4, 5-dihydro-1H-pyrazol-3-yl]-3-(4-chlorophenyl) sydnone **2a**	3263.93 (N–H), 1735.62 (C=O), 3057.58 (CH, pyrazoline)	3.38 (-OCH_3), 3.171 (1H, 5CH, pyrazoline) 6.72-7.98 (4H, 4H 2Ar-H), 13.2 (1H,-NH).	40.08, 55.14 (-OCH_3), 95.13, 111.74, 114.13, 118.28,123.44, 126.99, 128.45, 129.03, 130.19, 159.25, 168.40	$C_{18}H_{15}ClN_4O_3$, Mol. wt. 370.79 Mass: 370.08 m/z=370.00 C, 58.29; H, 4.13; N, 15.14. % Yield=71, Rf=0.513 mp=129–131°C.
Synthesis of 4-[5-(4-methoxyphenyl)-4, 5-dihydro-1H-pyrazol-3-yl]-3-(4-fluorophenyl) Sydnone **2b**	1735.62 (C=O), 3262.83 (NH pyrazoline)	7.07 (C_6H_{4F}, 2H) 7.2 (C_6H_4F, 2H) 7.07 (N-H, 1H) 6.91 (C_6H_4, 2H) 6.93 (C_6H_4, 2H) 3. 38(OCH_3, 3H) 3.17 (pyrazole, 5CH, 1H) 8.5 (1H), 13.2 (1H, NH)	116-162 (C_6H_4F), 113.9-160 (C_6H_4), 55.14 (OCH_3), 40.08 (pyrazole, 4C), 49.1(pyrazole, 5C), 159.6 (pyrazole, 3C), 95.13(sydnone, 5C), 123 (sydnone, 4C), 168	$C_{18}H_{15}FN_4O_3$ Mol. wt.-354.34 m/z= 354.11, C, 61.01; H, 4.27; N, 15.81. % Yield=69, Rf=0.539 mp=132–133°C
Compound with IUPAC name	**IR (KBr) (cm^{-1})**	**^{1}H NMR (δ ppm)**	**^{13}C NMR (δ ppm)**	**Physicochemical data**
4-[5-(4-methoxyphenyl)-4, 5-dihydro-1H-pyrazol-3-yl]-3-(2,4-dichlorophenyl) sydnone **2c**	3285.23 (N–H), 1721.47 (C=O).	7.1- 7.3 ($C_6H_3Cl_2$, 3H) 7.0 (N-H, 1H) 7.01 ($C_6H_4OCH_3$, 2H) 6.72 ($C_6H_4OCH_3$, 2H) 3.9 (Pyrazole, 5CH, 1H) 3.73 (OCH_3, 3H) 1.9 (Pyrazole, $4CH_2$, 2H).	40 (pyrazole, 4C), 53.4(pyrazole, 5C), 56 (OCH_3), 105.7(sydnone, 5C), 121.67 (sydnone, 4C), 127-135 ($C_6H_3Cl_2$), 155.6 (pyrazole, 3C), 113.9-160 ($C_6H_4OCH_3$)	$C_{18}H_{14}Cl_2N_4O_3$ Mol. wt.:405.235, m/z= 404.044, C, 53.35; H, 3.48; N, 13.83 % Yield=73, Rf*=0.548 mp=131–133°C.
4-[5-(4-methoxyphenyl)-4,5-dihydro-1H-pyrazol-3-yl]-3-(4-bromophenyl)sydnone **2d**	1735.29 (C=O), 3263.93 (NH pyrazoline)	7.0 (C_6H_4Br, 2H) 7.2 (C_6H_4Br, 2H) 7.0 (N-H, 1H) 6.72 (C_6H_4, 2H) 7.01 (C_6H_4, 2H) 3. 38(OCH_3, 3H) 3.17 (Pyrazol, 5CH, 1H) 8.5 (1H), 13.2 (1H, NH)	116-162 (C_6H_4Br), 113.9-160 (C_6H_4), 55.14 (OCH_3), 40.08 (pyrazole, 4C), 49.1(pyrazole, 5C), 159.6 (pyrazole, 3C), 95.13(sydnone, 5C), 123 (sydnone, 4C), 168	$C_{18}H_{15}BrN_4O_3$ Mol. wt. 415.241, m/z= 414.4, C, 52.06; H, 3.64; N, 13.49 % Yield=79, Rf=0.613 mp=146–148°C.
Compound with IUPAC name	**IR (KBr) (cm^{-1})**	**^{1}H NMR (δ ppm)**	**^{13}C NMR (δ ppm)**	**Physicochemical data**
4-[5-(furyl)-4, 5-dihydro-1H-pyrazol-3-yl]-3-(4-chlorophenyl) sydnone **2e**	3263.63 (N–H), 1735.28 (C=O)	3.19(d, 1 H), 3.45 (s, 3 H), 6.79 (d, 2 H) 7.03 (d, 2 H), 7.38 (d, 2 H), 7.55 (d, 2 H), 7.71 (d, 1 H), 8.10 (d, 2 H)	40.06, 95.07, 123.32, 130, 133, 136, 147, 160, 168	$C_{15}H_{11}ClN_4O_3$ Mol. wt. 330.726 Mass: 330.052, m/z: 330.052, C, 54.47 H, 3.35; N, 16.94 % Yield=64, Rf=0.609 mp=155–158°C
4-[5-(furyl)-4,5-dihydro-1H-pyrazol-3-yl]-3-(4-fluorophenyl)sydnone **2f**	1735.89 (C=O), 3263.93 (NH pyrazoline)	7.0 (C_6H_4F, 2H) 7.2 (C_6H_4F, 2H) 7.0 (N-H, 1H) 6.06 (Furyl, 3CH, 1H) 6.24 (Furyl, 4CH, 1H) 7.28 (Furyl, 5CH, 1H) 3.9 (Pyrazol, 5CH, 1H) 1.9 (Pyrazol, $4CH_2$, 2H)	41.0 (pyrazole, 4C), 48.8(pyrazole, 5C), 105.7(sydnone, 5C), 121.67 (sydnone, 4C), 116-162 (C_6H_4F), 155.6 (pyrazole, 3C), 104.9-157.6 (furyl, C_4H_3O)	$C_{15}H_{11}FN_4O_3$ Mass: 314.08 Mol. wt. 314.27, m/z = 314.082, C, 57.29; H, 5.56; N, 17.88 % Yield=70, Rf=0.0.57 mp=143–145°C

Compound with IUPAC name	IR (KBr) (cm^{-1})	^{1}H NMR (δ ppm)	^{13}C NMR (δ ppm)	Physicochemical data
4-[5-(furyl)-4, 5-dihydro-1H-pyrazol-3-yl]-3-(2,4-dichlorophenyl)sydnone **2g**	1731.18 (C=O) 3261.05 (NH pyrazoline)	7.1- 7.3 ($C_6H_3Cl_2$, 3H) 7.28 (furyl, 5CH, 1H), 7.1 (N-H, 1H), 6.24 (furyl, 4CH, 1H) 6.06 (furyl, 3CH, 1H) 4.1(Pyrazole, 5CH, 1H) 1.9 (Pyrazole, $4CH_2$, 2H)	38 (pyrazole, $4CH_2$), 53.1(pyrazole, 5C), 105.7(sydnone, 5C), 121.67 (sydnone, 4C), 127-135 ($C_6H_3Cl_2$), 155.6 (pyrazole, 3C), 104.9 (furyl, 3C), 110 (furyl, 4C), 140.6(furyl, 5C), 157.6(furyl, 2C)	$C_{15}H_{10}Cl_2N_4O_3$ Mol. wt. 365.171, m/z= 364.013, C, 49.34; H, 2.76; N, 15.34 % Yield=63, Rf=0.535 mp=196–198°C
4-[5-(furyl)-4,5-dihydro-1H-pyrazol-3-yl]-3-(4-bromophenyl) sydnone **2h**	1733.35 (C=O), 3262.30 (NH pyrazoline)	7.0 (C_6H_4Br, 2H) 7.2 (C_6H_4Br, 2H) 7.0 (N-H, 1H) 6.06 (Furyl, 3CH, 1H) 6.24 (Furyl, 4CH, 1H) 7.28 (Furyl, 5CH, 1H) 3.9 (Pyrazol, 5CH, 1H) 1.9 (Pyrazol, $4CH_2$, 2H)	40.06 (pyrazole, 4C), 95.07(sydnone, 5C), 123 (sydnone, 4C), 130-160 (C_6H_4F), 155.6 (pyrazole, 3C), 104.9-157.6 (furyl, C_4H_3O), 168.11	$C_{15}H_{11}BrN_4O_3$ Mol. wt.: 375.177, m/z= 375, C, 48.02; H, 2.96; N, 14.93 % Yield=59, Rf=0.49 mp=163-165°C
Compound with IUPAC name	**IR (KBr) (cm^{-1})**	**^{1}H NMR (δ ppm)**	**^{13}C NMR (δ ppm)**	**Physicochemical data**
4-[5-(4-nitrophenyl)-4, 5-dihydro-1H-pyrazol-3-yl]-3-(4-chlorophenyl) sydnone **2i**	3585.65 (N–H), 1735.87 (C=O)	3.17 (d, 1 H), 3.41 (d, 1 H), 4.76 (t, 1H), 6.84 (d, 2 H), 7.21 (d, 2 H), 7.68 (d, 2H), 7.98 (d, 2H), 8.12 (d, 1 H)	39.64, 40.06, 123.38, 123.69, 130.17, 144.18, 149.98, 165, 168	$C_{17}H_{12}ClN_5O_4$ Mol. wt. 385.761, m/z: 385.058, C, 52.93; H, 3.14, N, 18.15, % Yield=63, Rf=0.58 mp=157-159°C
4-[5-(4-nitrophenyl)-4,5-dihydro-1H-pyrazol-3-yl]-3-(4-fluorophenyl)sydnone **2j**	1735.33 (C=O), 3113.21(NH pyrazoline).	8.14 ($C_6H_4NO_2$, 2H) 7.38 ($C_6H_4NO_2$, 2H) 7.2(C_6H_4F, 2H), 7.3 (C_6H_4F, 2H) 8.14 ($C_6H_4NO_2$, 2H) 7.38 ($C_6H_4NO_2$, 2H) 7.0 (Pyrazole, N-H, 1H) 3.9 (Pyrazol, 5CH, 1H) 1.9 (Pyrazol, $4CH_2$, 2H)	116-162 (C_6H_4F), 123.4-148.5 (C_6H_4), 43 (pyrazole, 4C), 49.1(pyrazole, 5C), 155.6 (pyrazole, 3C), 105.7(sydnone, 5C), 121.67 (sydnone, 4C)	$C_{17}H_{12}FN_5O_4$, Mol. wt. 369.307, m/z= 369.087, C, 55.29; H, 3.28; N, 18.96 % Yield=81, Rf=0.534 mp=145-149°C

Compounds 6a-x are soluble in DMSO
* Rf values are taken in benzene: ethyl acetate (8.5:1.5 v/v)

Anti-cancer screening

'Brine shrimp lethality bioassay' (Preliminary cytotoxicity study)

Screened against a panel of 60 different human tumor cell lines (*In-vitro* study)

Preliminary anticancer activity by Brine shrimp lethality bioassay (Meyer et al 1982, Zhao et al 1992)

Performed using Meyer's method. The lethal concentrations resulting in 50% mortality of the brine shrimp (LC_{50}) was determined from the 24h counts. The dose-response data were transformed into a straight line through trade line fit linear regression analysis. It reported in Table 2).

Table 2 Brine Shrimp lethality assay of compounds **2a-j**

Comp.	**LC_{50}(µg/ml)**
2a	11.65
2b	13.45
2c	12.45
2d	15.11
2e	12.45
2f	14.74
2g	13.09
2h	15.71

2i	07.45
2j	09.66

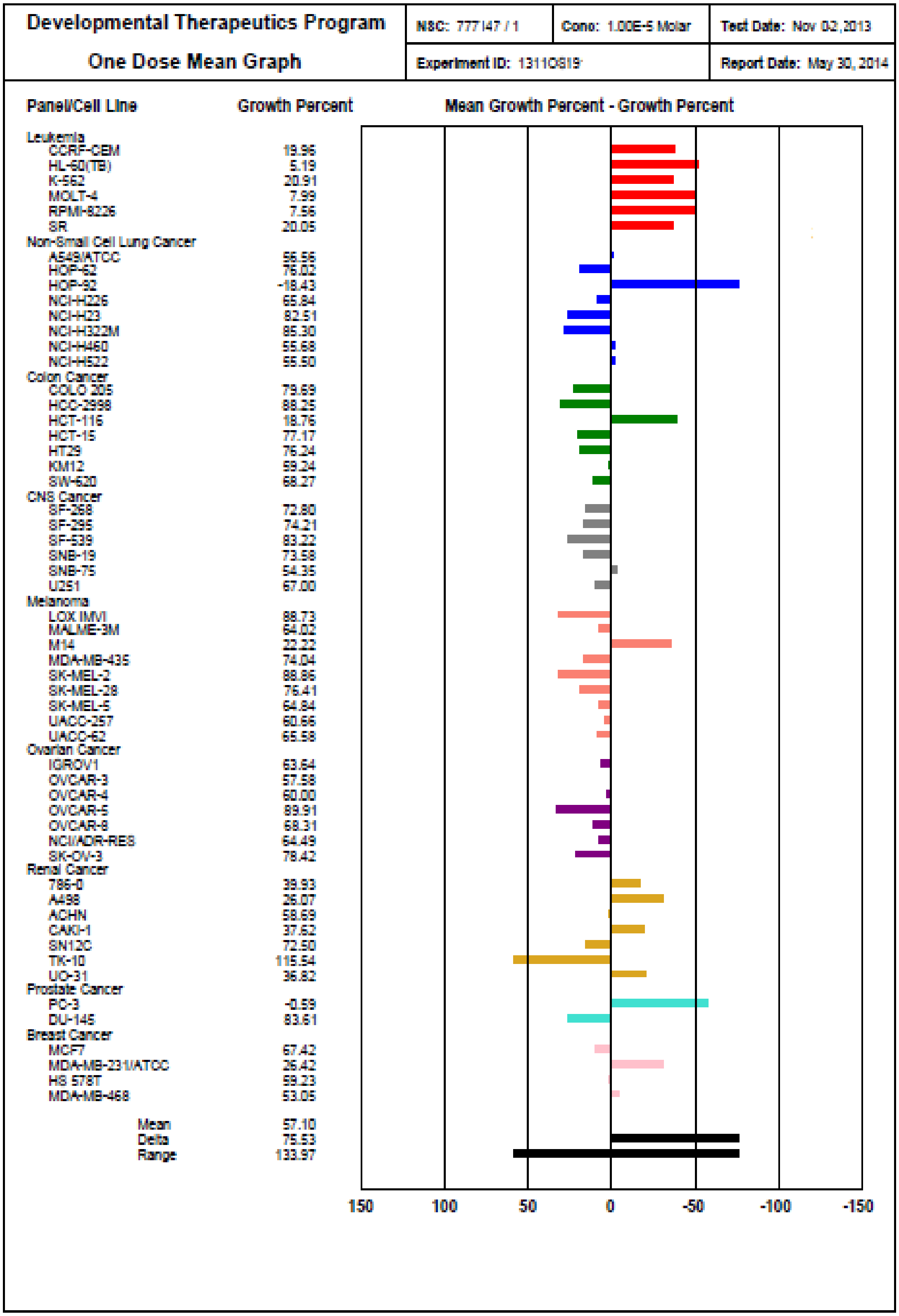


Figure 5 Anticancer activity for **2i** against 60 human cancer cell lines

***In-vitro* anticancer evaluation against 60 human tumor cell lines** (Adams et al, 2005; Al-Suwaidan et al, 2013; Lorenzi et al, 2009; Mingyi et al, 2013; Roschke et al, 2003; Dudhe et al, 2014)

Evaluation of compounds **2i, 2j** for anticancer activity was done at NCI, Bethesda, USA as per standard procedure. The screening was performed against various nine neoplastic cancers cell lines (leukemia, non-small cell lung, colon, CNS, melanoma, ovarian, renal, prostate and breast cancers). The results recorded as a mean graph for % growth inhibition of treated cells and represented as one dose DTP curve and is shown in Fig. 5-6.

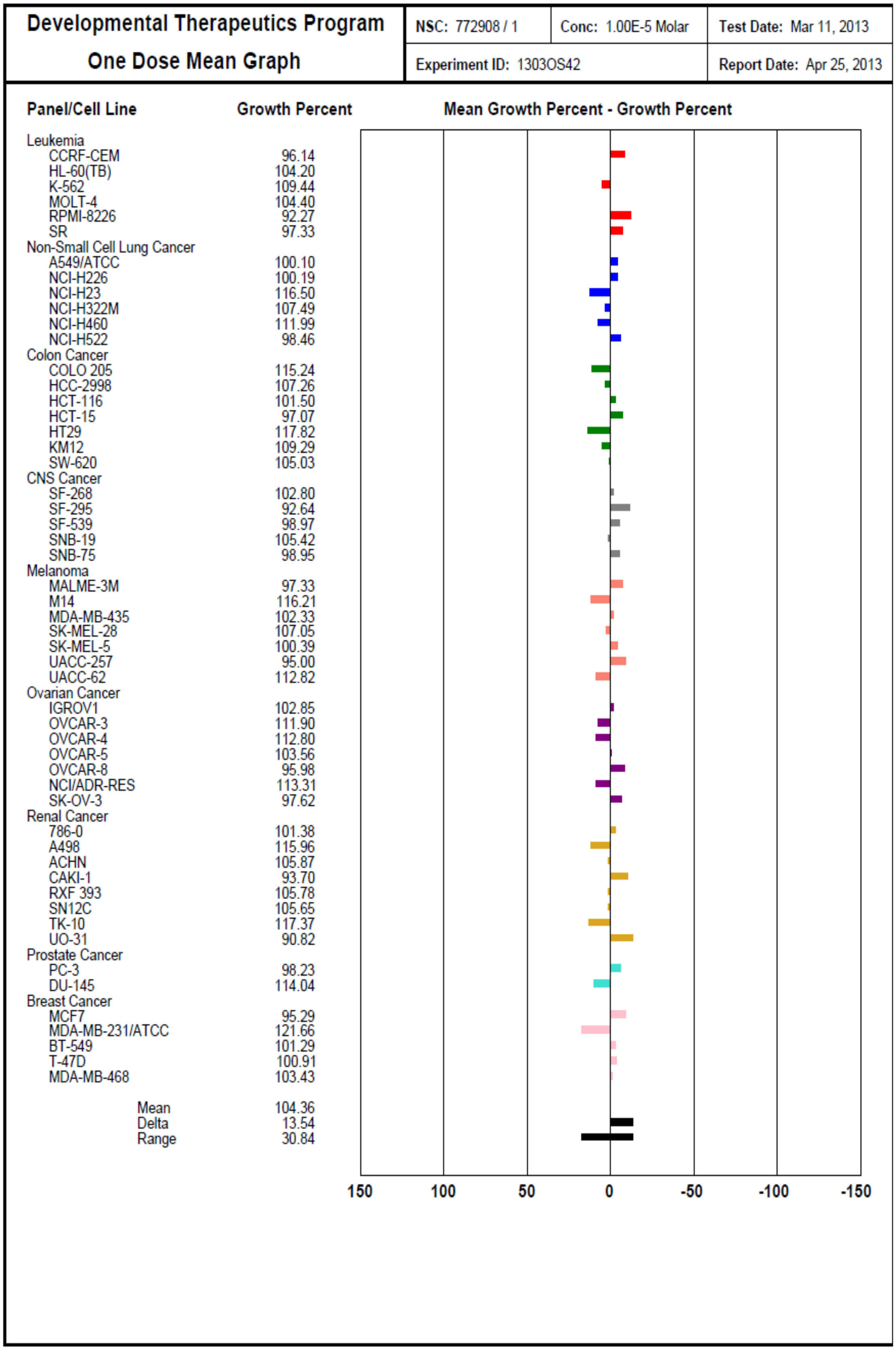


Figure 6 Anticancer activity for **2j** against 60 human cancer cell lines

Table 3 Anticancer screening data for compound **2i, 2j**

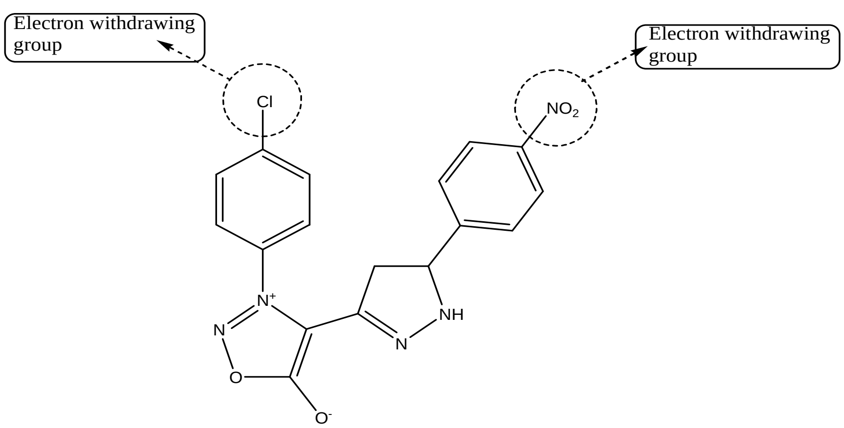
Human tumor cell line	% GI for 2i	% GI for 2j	% GI for Std.
	Leukemia		
CCRF-CEM	37.17	4.49	4.49
HL-80	51.19	-	35.39
K-562	36.19	-	10.89
MOLT-4	49.11	-	5.30
RPMI-8226	49.44	12.09	16.2
SR	37.05	7.03	0.5
	Non-Small Cell Lung Cancer		
HOP-92	75.53	-	-62.00
A549/ATCC	-	4.26	-6.3
NCI-H226	-	4.17	-.17.9
NCI-H23	-	-12.14	-280.1
NCI-H322M	-	-3.13	-33.4
NCI-H460	-	-7.63	13.00
NCI-H522	-	-5.90	23.4
	Colon Cancer		
HCT-116	38.34	-	47.00
HCT-15	-	7.29	-0.6
SW-620	-	-	-5.2
	CNS Cancer		
SNB-75	2.75	-	-5.4
SF-295	-	11.72	-3.3
SF-268	-	-	-13.6
	Melanoma		
M-14	34.88	-	ND
MALME-3M	-	7.03	-35.1
UACC-257	-	10.34	4.6
	Ovarian Cancer		
OVCAR-04	-2.90	-	-38.9
OVCAR-8	-	8.38	ND
SK-OV-3	-	6.74	18.2
IGROV1	-	-	6.3
	Renal Cancer		
786-0	17.17	-	-2.1
A498	31.03	-	ND
CAKI-1	19.48	10.66	-16.2
UO-31	20.28	13.54	-18.3
SN-12C	-	-	-29.6
	Prostate Cancer		
PC-3	57.69	6.13	-8.00
	Breast Cancer		
MDA-MB-231/ATCC	30.68	-	37.4

MCF7	-	10.34	7.9
BT-549	-	-	34.5
T-47D	-	-	-48.5
Mean	57.10	104.36	10.298
Delta	75.53	13.54	83.798
Range	133.97	30.84	363.9

Range = highest growth percent- lowest growth percent.
Delta = mean growth percent - lowest growth percent.
% GI: % growth inhibition = mean growth percent- % growth,
Standard –Vincristine sulphate, ND-not determined, -- poor GI

CONCLUSION

Based on *in-vitro* evaluation, compound **2i** showed higher and broader spectrum of anticancer activity against leukemia (all cell lines), non-small cell lung cancer (HOP-92), prostate cancer (PC-3), melanoma (M14), renal cancer (786-O, A498, CAKI-1, UO-31 cancer cell lines), prostate cancer (PC-3) as compared to standard and **2j** (as shown in Fig. 5 and Table 3). Compound **2i** showed prominent anticancer activity due to active sydnone ring and substitution of 3rd and 4th position of sydnone with aryl ring having electron withdrawing functional groups like chloro (-Cl) and nitro ($-NO_2$) which make benzene ring more stable and may also increases lipophilicity to penetrate easily into cancer cells. Compound may exhibited anticancer activities over multiple mechanisms with inhibiting protein kinase (CDK, MK-2, PLK1, kinase-like protein Eg5 and IKK), topoisomerase I and II, microtubule inhibition and many others. (Jawaid et al, 2000) Further research and development with designing necessary structural modifications of molecule **2i**may lead to safer and effective potential anticancer drug candidates. The finding of the study inferred that the molecule **2i**renders as a lead for further development of novel potent anticancer molecules against specific tumor cell line.



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